

1 **REMARKS**

2 Applicant has carefully considered the positions of the Examiner and respectfully
3 requests reconsideration based upon the manifest differences between the present invention and
4 the cited references. In the June 16, 2004, Office Action the Examiner rejected claims 1-29
5 under 35 U.S.C. §§ 112 and/or 103. Applicant herein responds to those rejections and highlights
6 the differences between the pending claims and the cited references such that it should become
7 apparent to the Examiner that these rejections should be reconsidered and withdrawn.

8 In the Office Action dated June 16, 2004, the Examiner rejected Claims 15, 18, 21, 24
9 and 27 under 35 U.S.C. § 112, and Claims 1-29 under U.S.C. § 103 as unpatentable over Yates,
10 *J. Mass Spectrom.*, Vol. 33, 1-19, 1998, ("Yates") and/or Franzen et al. U.S. Patent No.
11 5,663,561 ("Franzen") in view of Dasseux et al. U.S. Patent Application Serial No. 09/735,707
12 ("Dasseux"). Applicant respectfully submits the Examiner's reliance upon the cited references is
13 misplaced as Applicant's invention is very different from what is disclosed therein. In particular,
14 Applicant would like to direct the Examiner's attention to applicant's novel system and method
15 for analyzing a complex biological sample, which allows for identification of all cellular
16 components, including, but not limited to, drug metabolites, proteins and small molecules by
17 precisely determining the molecular weight and empirical formulae of these compounds.

18 Specifically, the present invention discloses a method for analyzing complex biological
19 samples, such as drug-dosed cellular samples, using a Fourier Transform Mass Spectrometer
20 (FTMS). The preferred method comprises the steps of ionizing the drug-dosed sample to
21 produce sample ions, introducing said sample ions into an analysis region of said Fourier
22 Transform Mass Spectrometer, analyzing said sample ions to determine the molecular weight

1 and abundance of said sample ions, utilizing said molecular weight to determine the molecular
2 formula of each species of said sample, and identifying each of said species by comparing said
3 empirical formula to a database of formulas for known molecules.

4 Initially the Examiner rejected claims 15, 18, 21, 24 and 27 under 35 U.S.C. § 112 as
5 failing to comply with the written description requirement because the claims contain subject
6 matter not described in the specification in such as way as to reasonably convey to one skilled in
7 the relevant art that the inventors, at the time the application was filed, had possession of the
8 claimed invention. Applicant respectfully disagrees. In particular, Applicant submits that the
9 Examiner's opinion that "[t]he instant specification does not disclose injecting a drug into a
10 biological sample" is incorrect. Rather, Applicant submits that the claims are supported by the
11 specification and directs the Examiner's attention to page 1, lns. 5-9, and page. 12, ln. 19 through
12 page.13, ln. 2 of the originally filed application. Specifically, Applicant discloses "a Fourier
13 transform mass spectrometry (FTMS) system or similar devices to utilize ultra high resolution
14 and sensitivity to detect drug metabolites in cell extracts. This allows the present invention to
15 detect drug metabolites, in vitro, under high throughput conditions, thereby providing a means
16 for the rapid screening of drug dosed, biological samples." (Emphasis added). The disclosure
17 further provides "while the monitoring of predicted drug metabolites in biological fluids is
18 practiced throughout the industry, the monitoring and characterization of all chemical changes in
19 a cell following drug dosage has never been accomplished. The method of the present invention
20 includes analyzing a biological sample using a Fourier transform Mass spectrometer." (Emphasis
21 added). The testing of drug dosed biological samples is clearly disclosed in the present
22 application as to reasonably convey that the invention teaches a means of screening drug-dosed

1 biological samples and that the samples prepared by injecting drugs into test cells are inherently
2 biological in nature. Applicant therefore respectfully requests that this rejection be withdrawn.

3 Next, the Examiner rejected claims 1-11 and 15-26 under 35 U.S.C. § 103(a) as being
4 unpatentable over Yates in view of Dasseux. Applicant respectfully disagrees and submits that
5 the Examiner's application of the teachings of the cited references is misplaced. Specifically,
6 applicant disagrees with the Examiner's characterization of the specific teachings of Yates and
7 Dasseux and any combination thereof. More importantly, even if the cited references were
8 properly combined, such a combination would not teach all of the novel and non-obvious
9 features of the present invention as claimed.

10 Initially, the Examiner applies Yates as in the Office action mailed October 30, 2003. In
11 particular, the Examiner cites that Yates teaches "utilizing said molecular weight to determine
12 the empirical formula of each species of said sample and identifying each said species by
13 comparing said empirical formula to a database of formulas for known molecules." Applicant
14 respectfully disagrees. Rather, Yates merely teaches using mass spectrometry to identify a single,
15 purified sample of a specific protein, and fails to teach a method for characterizing each species.
16 Further, Yates does not use molecular weight to determine the empirical formula of each species
17 present in a sample, but instead uses the molecular weight determination of the protein to narrow
18 the list of possible sequence possibilities. According to Yates, the predicted fragment ions for
19 each of the amino acid sequences matching the mass of the peptide to those observed in the
20 tandem mass spectrum is correlated (See Yates, pg. 9, col. 2). Thus, an empirical formula is not
21 calculated from the molecular weight of the species, nor is it used to identify the compound in
22 the teachings of Yates, as claimed in the subject application.

1 Applicant further submits that the Examiner's reliance on Dasseux with respect to the
2 rejections of claims 1-11 and 15-26 under 35 U.S.C. § 103 is misplaced. In the opinion of the
3 Examiner, "Dasseux teaches analyzing biological samples using FTMS, wherein prior to analysis
4 by FTMS, either cell lysates (biological samples) or intact cells are treated with drugs."
5 However, Applicant submits that Dasseux fails to teach several aspects of the presently claimed
6 invention. Specifically, Dasseux does not teach using the molecular weight to determine the
7 empirical formula of each species present in a said sample, nor identifying each said species.
8 Rather, Dasseux simply teaches a method for analyzing drug-dosed biological samples using
9 FTMS, whereby peak profiles are acquired and are used to detect phenotypic differences
10 associated with drug-dosing. In short, Dasseux teaches a method that permits the elucidation of
11 molecular differences between complex biological samples, but does not permit the
12 determination of the molecular weight and empirical formula of each species present in the
13 sample.

14 Importantly, Dasseux also teaches away from the methods claimed in the present
15 invention. That is, Applicant directs the Examiner's attention to paragraph 0131 of Dasseux,
16 which states that "[m]ost biological molecules corresponding to peaks observed in this type of
17 analysis are not identifiable, at least initially, until databases of HICS-FTMS peak profiles and
18 the identities of molecules corresponding to those individual peaks are compiled (Page 13, lines
19 41-46). According to Dasseux, these peaks are unidentifiable, whereas the present invention
20 claims a method to identify these peaks. In view of the above, the applicant respectfully requests
21 that this rejection be withdrawn.

22 Lastly, the Examiner also rejected Claims 12-14 and 27-29 under 35 U.S.C. § 103 as

1 being unpatentable over Yates and Franzen in view of Dasseux. Applicant respectfully submits
2 that the Examiner's application of the teachings of Yates and Dasseux are misplaced for reasons
3 discussed above. Furthermore, an examination of Franzen reveals that only a method of ionizing
4 large, non-polar molecules at atmospheric pressure is taught. As stated previously, Franzen does
5 not disclose any techniques for compound identification or empirical formula determination.
6 Thus, Franzen adds nothing new to the teachings of Yates and Dasseux, and these references,
7 either alone or in combination, fail to teach the limitations of the pending claims. Specifically,
8 none of the references teach that the molecular weights of all the components of a drug-dosed
9 biological sample are utilized to identify the empirical formulae of those components.
10 Therefore, the applicant submits that the rejection of claims 12-14 and 27-29 under 35 U.S.C. §
11 103 as being unpatentable over Yates and Franzen in view of Dasseux should be reconsidered
12 and withdrawn.

13 Therefore, as is evidenced by the above remarks, the present invention, for the first time,
14 discloses a method for the analysis of biological samples using FTMS which allows for the
15 constant and immediate monitoring of the effects of drugs on a sample and permits identification
16 of all sample components.

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Date: December 16, 2004

Respectfully Submitted,

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